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Ultrasound-guided unilateral neck exploration for sporadic primary hyperparathyroidism: is it worthwhile?

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The role of preoperative localisation tests before initial neck exploration for primary hyperparathyroidism (PHP) remains controversial, as does the optimal surgical approach. We report our experience with preoperative ultrasound (US) and the operative management of sporadic PHP between 1990 and 1995. Preoperative US was carried out by an experienced radiologist. Three surgeons adopted a policy of 'selective' US-guided unilateral neck exploration (UNE); the fourth surgeon performed routine bilateral neck exploration (BNE). There were 72 patients: 26 men and 46 women, with a mean age of 57.4±12.5 years (range 21–80 years). All patients underwent initial neck exploration for 'sporadic' PHP, of whom 63 had preoperative US. This was positive in 52 patients; 27 of whom underwent a UNE, 23 had a BNE, and two patients had a UNE converted to a BNE. Patients with 'negative' US ($n=11$), and those receiving no preoperative localisation test ($n=90$) underwent a BNE. The sensitivity, specificity and accuracy of US were 80% (52/65), 100% (61/61), and 90% (113/126), respectively. Comparable success rates were achieved (BNE: 97% (33/34) *vs* UNE: 93% (27/29), $P<0.05$), with very low morbidity. Failures with the scan-guided UNE were caused by missed contralateral adenomas. An experienced radiologist and a low incidence of multiglandular disease (MGD) are essential prerequisites for the scan-guided unilateral approach. An experienced surgeon, on the other hand, is the only prerequisite for the 'gold standard' bilateral approach.

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Endocrine surgeons generally agree on the indication for localisation tests before re-exploration of the neck for persistent or recurrent primary hyperparathyroidism (PHP) *(1–3)*. However, the role of these tests before initial neck exploration for PHP remains controversial, mainly because of disagreement among surgeons as to the optimal surgical approach in these patients *(4,5)*.

Bilateral neck exploration (BNE) with identification of all four parathyroid glands is considered by most to be the 'gold standard' *(6–7)*, achieving high success rates *(8–13)* with very low morbidity rates *(1,4)*. However, advocates of the selective unilateral neck exploration (UNE) approach *(15–19)* argue that since a single adenoma is the culprit in 80–90% of patients with sporadic PHP *(8,9,13,20)* its preoperative localisation to one side of the neck could save an unnecessary controlateral exploration. This, it is argued, would reduce operative time *(15–17,21,22)* and the incidence of postoperative complications, and facilitate reoperative surgery on the unscarred side of the neck. High-resolution, real-time ultrasound (US) has emerged in recent years as the ideal tool for the

job, being non-invasive, relatively inexpensive and less time-consuming than other localisation tests. However, several investigators questioned its suitability as a routine preoperative localisation tool *(23,24)* and its cost-effectiveness *(25)*, while others failed to demonstrate a significant reduction in operative time *(10,26)* and costs *(10,23,27)* with the 'scan-directed' UNE approach. More importantly, its critics raised concerns about missed multiglandular disease (MGD) *(7)*, noting that this pathology has often been missed by preoperative localisation tests *(25)*. Our experience with preoperative US localisation, and the two schools of surgery for sporadic PHP is here presented.

Methods

Patients

During the 6-year period, between January 1990 and December 1995, a total of 72 consecutive patients with sporadic PHP underwent 'initial' neck exploration at Bradford Royal Infirmary. The diagnosis of 'sporadic' PHP was based on the persistent rise in fasting serum calcium and parathyroid hormone levels, and the absence of a personal or family history suggestive of familial hyperparathyroidism or multiple endocrine neoplasia.

There were 26 men and 46 women, with a mean age of 57.4±12.5 years (range 21–80 years). Of these, 63 patients had attempted preoperative localisation of enlarged parathyroid gland(s) using ultrasonography. The remaining nine patients had no preoperative localisation studies performed.

Ultrasonography

Ultrasonographic examinations were all performed by one consultant radiologist (TDG) who had a special interest in this field, using 7–10 MHz real-time scanner (Ultramark-9 HDI, Advanced Technology Laboratories UK Ltd, Letchworth, Herts). Patients were positioned supine with their neck extended and a pillow placed under the shoulders. Longitudinal and transverse sonograms of the anterior neck were obtained extending from hyoid bone to sternal notch, carefully recording the location (side: right/left, site: upper/lower) of any detected enlarged parathyroid gland, and its three dimensions whenever possible. The thyroid gland was also examined in all cases, recording any abnormality.

Surgery

All patients underwent 'initial' neck exploration under general anaesthesia. Three surgeons adopted a policy of US-guided UNE. Thus, the side identified at preoperative US to contain an enlarged parathyroid gland was explored first and the enlarged gland removed. The ipsilateral parathyroid gland was then explored; if this appeared normal it was not biopsied and the exploration was terminated, but if enlarged or could not be found a contralateral exploration was performed. Failure to achieve preoperative localisation (US not performed, or reported as 'negative' or 'normal') resulted in a routine BNE. The fourth surgeon adopted a policy of 'universal' BNE regardless of the US localisation result. No biopsies of normal-looking glands were obtained. All surgeons performed $3\frac{1}{2}$ subtotal parathyroidectomy whenever four-gland hyperplasia was suspected, leaving a remnant *in situ* equivalent to a normal-sized parathyroid gland.

Operative details were carefully recorded with special attention to the side and site of any enlarged parathyroid gland removed, the number and location of normal gland(s), the side(s) explored, any associated thyroid disease and any additional thyroid surgery simultaneously performed.

Operative failure was defined as either 'persistent' hyperparathyroidism (hypercalcaemia occurring within 6 months of operation) or 'recurrent' hyperparathyroidism (onset of hypercalcaemia more than 6 months after operation).

Localisation analysis

A 'true-positive' test indicates the finding at neck exploration of an enlarged/abnormal parathyroid gland on the same 'side' as indicated by preoperative US. A 'true-negative' test indicates the absence of an enlarged/abnormal parathyroid gland at neck exploration on the side reported by preoperative US as 'negative' or 'normal'. The 'sensitivity' of US was calculated as the number of true-positive tests divided by the actual number of sides with abnormal parathyroid gland(s) as found either at initial neck exploration or at postoperative further localisation studies with or without confirmatory re-exploration after failed initial neck exploration. The 'specificity' of US was calculated as the number of true-negative tests divided by the total number of sides carrying no abnormal glands as confirmed by surgical exploration in those who underwent BNE, or by the absence of disease recurrence at follow-up in those who underwent UNE. The 'accuracy' of US was calculated as the true-positive and true-negative results divided by the total number of sides examined.

Follow-up

Regular follow-up was achieved on all patients, checking serum calcium levels at each visit to detect early and late recurrences. Mean follow-up was 3.7 years (range 10 months to 6 years).

Results

Ultrasound 'positive' patients

Preoperative US was positive in 52 of 63 patients (82.5%), detecting a solitary parathyroid gland enlargement in all 52 patients. Of these, 29 patients were admitted for UNE and 23 for BNE. UNE was achieved in 27 of 29 patients, the remaining two were converted to a BNE. Conversions were owing to failure to identify an ipsilateral parathyroid

gland in one patient (finding two normal contralateral glands) and the finding of a four-patient hyperplasia in the other (Table I).

In 50 of these 52 patients, a single enlarged parathyroid gland was detected at surgery; all were correctly localised to side by preoperative US, and all but two were correctly localised to site. In the remaining two patients, four-gland hyperplasia was detected at surgery. The rate of true-positive US tests was 100% (52 of 52 sides).

Hypercalcaemia was corrected in all 52 patients, but recurred at 1 month and 3 months postoperatively (persistent hypercalcaemia) in two patients who underwent UNE. Further postoperative localisation studies (selective venous sampling, CT scan, radioisotope scan) demonstrated a contralateral 'adenoma' in both patients; this was confirmed at re-exploration in one patient (1 cm, 400 mg), the other refused further surgery.

Ultrasound 'negative' patients

In the remaining 11 of 63 patients (17.5%), preoperative US failed to demonstrate an enlarged parathyroid gland, and were therefore reported as 'normal' or 'negative'. All underwent BNE, detecting a single enlarged parathyroid gland in the neck of nine patients (adenoma, 8; hyperplasia, 1), and a 'cervical' superior mediastinal adenoma in one. No abnormal parathyroid gland was found in one patient (negative/failed exploration), in whom subsequent localisation studies demonstrated a superior mediastinal 'adenoma'. He refused further surgery.

Negative US was associated with inaccessible enlarged parathyroid gland in three patients (two superior mediastinum: 1.1 g, 2 g; one retro-oesophageal: 700 mg), multinodular goitre in four (two ipsilateral unilobar disease: 600 mg, 1.3 g; two bilobar disease: 1 g, 1.7 g), a small adenoma (0.7 cm, 100 mg) in one, extensive degenerative changes within an adenoma (1.5 cm, 300 mg) in one, a single gland hyperplasia (1.0 cm, 900 mg) in one, and a large adenoma (2 cm, 1.2 g) in one.

Overall results

The sensitivity, specificity and accuracy of US were 80% (52/65), 100% (61/61), and 90% (113/126), respectively. The rates of false-positive and false-negative were 0.0% (0/52) and 20% (13/65), respectively.

The overall success rate of initial neck exploration for sporadic PHP in this series was 96% (69/72). When the results were analysed on 'intention to treat' basis, a higher success rate was achieved with BNE compared with UNE (93% (27/29) *vs* 97% (33/34)). However, the difference was not statistically significant ($P > 0.05$).

Morbidity and mortality

Postoperative complications were encountered in three patients (4%). One patient developed a wound haematoma after UNE that resolved with conservative treatment. Two patients developed symptomatic transient hypocalcaemia requiring short-term replacement therapy; one followed a UNE and removal of a 5.2 g adenoma, the other complicated a BNE with excision of a 4.6 g adenoma combined with total thyroidectomy for multinodular goitre. There were no operative deaths.

Pathology

The distribution of parathyroid disease in all 72 patients is summarised in Table II. The mean (±SD) weight of the pathological glands removed was 1.4 g±1.6 g (range 0.1–10.5 g). The mean weight of the removed parathyroid glands in ultrasound negative patients was 1±0.56 g, that of ultrasound positive patients was 1.5±1.7 g ($P = 0.04$, unpaired t test). The incidence of multiglandular disease and double adenomas was 7% (5/72) and 4.2% (3/72), respectively. Of 72 patients, 11 (15.3%) had thyroid disease detected on preoperative US, of whom seven had concomitant thyroid surgery.

Discussion

Accuracy of preoperative US for the localisation of abnormal parathyroid glands before initial neck exploration in patients with PHP varied widely among reports *(4,15,28)*, ranging between 43% and 92%. This largely depended on the interest and experience of the involved radiologist *(15,29)* and the incidence of MGD. Our series reports a high accuracy rate of 90% in patients with sporadic PHP in the hands of an experienced radiologist. This has permitted a high cure rate of 93% to be achieved in patients subjected to a US-guided UNE, which

Table I. Results of unilateral and bilateral neck exploration in 63 patients undergoing initial neck exploration for sporadic PHP

Operative approach	*Preoperative US*		*Recurrence*	*Negative exploration*
	Positive	*Negative*		
UNE	27	0	2	0
UNE→BNE	2	6	0	0
BNE	23	5	0	1
Total	52	11	2	1

UNE, unilateral neck exploration; BNE, bilateral neck exploration

Table II. Distribution of parathyroid disease in 72 patients with sporadic PHP

Parathyroid disease	*Type of neck exploration*			
	Preoperative US		*No US*	
	UNE	*BNE*	*BNE*	*Total (%)*
Single adenoma	25	32	7	64 (88.8)
Double adenoma	2*	0	1	3 (4.2)
Hyperplasia (1 PG)	1	1	1	3 (4.2)
Hyperplasia (4 PG)	0	2†	0	2 (2.8)
Carcinoma	0	0	0	0
Total	28	35	9	72

*Contralateral adenoma detected at re-exploration in one patient, and at relocalisation studies in the other patient

†In one patient a UNE was converted to BNE as two enlarged ipsilateral glands were detected

compares favourably with many others who routinely performed a BNE *(8,9,30)*. Asymmetric hyperplasia, reported by some as a potential cause for failure to explore the contralateral side of the neck if a scan-directed unilateral approach was adopted, did not feature in this series. The detection of two enlarged ipsilateral parathyroid glands at UNE resulted in a successful conversion to a BNE and the detection of four hyperplastic glands.

Previous reports demonstrate significant reductions in operative time with scan-guided UNE in comparison with the bilateral approach *(16,17,21,23,27,31)*, with mean time savings of 20–30 min. Further operative time savings can be achieved by omitting routine biopsy of the ipsilateral 'normal-looking' parathyroid gland for frozen-section examination at UNE. In our practice, as in others *(32)*, this conservative approach has not resulted in any missed ipsilateral pathological parathyroid gland.

All the above is attractive, but is it enough to render the unilateral approach worthwhile?

The bilateral approach achieved a higher cure rate when compared with the unilateral one (97% *vs* 93%), and at no extra morbidity. Several others report similarly high cure rates (95–98.5%) with the bilateral approach *(9–13,33,34)* and at a very low morbidity *(10,11)*.

We share the concerns of others *(7,25)* of the risk of missing contralateral disease when a scan-directed UNE is adopted. Double contralateral adenomas were missed both at preoperative scanning and at UNE in this series. We were particularly fortunate to have a low incidence for this pathology (4.3%). The incidence of MGD in general varies widely among reports *(6,9,12,17,35)*, ranging between 2% and 48% (7% in this series). It is generally lower if only sporadic PHP is considered, excluding the familial cases and those with MEN syndrome. The higher the incidence of MGD, the higher the expected surgical failure rate. These failures, often avoidable by careful BNE, add an appreciable burden as further localisation tests and surgery would follow, thus questioning the cost-effectiveness of preoperative US.

Various intraoperative manoeuvres were adopted to improve the detection rate of MGD and determine the extent of exploration. These include 'quick' PTH assay *(35,36)*, oil-red-O staining of frozen sections of normal-looking ipsilateral parathyroid gland *(18,20)*, and intraoperative US *(15)*. Some advocates of the unilateral approach have employed these techniques to determine the need for a contralateral exploration *(18,37)*. However, these require additional specialist expertise and add further to the operative time and cost, thus devaluing some of the arguments for the unilateral approach.

A high success rate can be achieved with the ultrasound-guided unilateral approach for sporadic PHP, which is comparable with that obtained with the standard bilateral approach. However, this requires the input of a skilled radiologist and a low incidence of bilateral adenomas as contralateral disease is often missed. On the other hand, an experienced surgeon is the only prerequisite to the high success and low morbidity rates achievable with bilateral neck exploration.

References

1 Clark OH, Okerlund MD, Moss AA *et al.* Localization studies in patients with persistent or recurrent hyperparathyroidism. *Surgery* 1985; **98**: 1083–94.

2 Rodriquez JM, Tezelman S, Siperstein AE *et al.* Localization procedures in patients with persistent or recurrent hyperparathyroidism. *Arch Surg* 1994; **129**: 870–75.

3 Shen W, Duren M, Morita E *et al.* Reoperation for persistent or recurrent primary hyperparathyroidism. *Arch Surg* 1996; **131**: 861–7.

4 Whelan PJ, Rotsein LE, Rosen IB *et al.* Do we really need another localizing technique for parathyroid glands? *Am J Surg* 1989; **158**: 382–4.

5 Tibblin S, Bondesson A-G, Uden P. Current trends in the surgical treatment of solitary parathyroid adenoma; a questionnaire study from 53 surgical departments in 14 countries. *Eur J Surg* 1991; **157**: 103–7.

6 Nottingham JM, Brown JJ, Bynoe RP, Bell RM, Haynes JL. Bilateral neck exploration for primary hyperparathyroidism. *Am Surg* 1993; **59**: 115–19.

7 Thompson NW. Localization studies in patients with primary hyperparathyroidism. *Br J Surg* 1988; 75: 97–8.

8 Russell CFJ, Edis AJ. Surgery for primary hyperparathyroidism: experience with 500 consecutive cases and evaluation of the role of surgery in the asymptomatic patient. *Br J Surg* 1982; **69**: 244–7.

9 Kaplan EL, Salti GI, Hara H, Ito K. Results and complications of the surgical treatment of primary hyperparathyroidism. *Ann Ital Chir* 1993; **64**: 365–70.

10 Roe SM, Burns RP, Graham LD, Brock WB, Russell WL. Cost-effectiveness of preoperative localization studies in primary hyperparathyroid disease. *Ann Surg* 1994; **219**: 582–6.

11 Van Heerden JA, Grant CS. Surgical treatment of primary hyperparathyroidism: an institutional perspective. *World J Surg* 1991; **15**: 688–92.

12 Summers GW. Parathyroid exploration. A review of 125 cases. *Arch Otolaryngol* 1991; **117**: 1237–41.

13 Shaha AR, Jaffe BM. Cervical exploration for primary hyperparathyroidism. *J Surg Oncol* 1993; **52**: 14–17.

14 Kjellman M, Sandelin K, Farnebo LO. Primary hyperparathyroidism: low surgical morbidity supports liberal attitude to operation. *Arch Surg* 1994; **129**: 237–40.

15 Lucas RJ, Welsh RJ, Glover JL. Unilateral neck exploration for primary hyperparathyroidism. *Arch Surg* 1990; **125**: 982–5.

16 Russell CFJ, Laird JD, Ferguson WR. Scan-directed unilateral cervical exploration for parathyroid adenoma: a legitimate approach? *World J Surg* 1990; **14**: 406–9.

17 Worsey MJ, Carty SE, Watson CG. Success of unilateral neck exploration for sporadic primary hyperparathyroidism. *Surgery* 1993; **114**: 1024–30.

18 Tibblin S, Bondeson AG, Ljungberg O. Unilateral parathyroidectomy in hyperparathyroidism due to single adenoma. *Ann Surg* 1982; **195**: 245–52.

19 Wang CA. Invited commentary: Unilateral neck exploration for primary hyperparathyroidism. *Arch Surg* 1990; **125**: 985.

20 Tibblin S, Bondeson AG, Bondeson L, Ljungberg O. Surgical strategy in hyperparathyroidism due to solitary adenoma. *Ann Surg* 1984; **200**: 776–84.

21 Wei JP, Burke GJ. Analysis of savings in operative time for primary hyperparathyroidism using localization with technetium 99m sestamibi scan. *Am J Surg* 1995; **170**: 488–91.

22 Arkles LB, Jones T, Hicks RJ, De Louisa MA, Chou ST. Impact of complementary parathyroid scintigraphy and ultrasonography on the surgical management of hyperparathyroidism. *Surgery* 1996; **120**: 845–51.

23 Hasselgren PO, Fidler JP. Further evidence against the routine use of parathyroid ultrasonography prior to initial neck exploration for hyperparathyroidism. *Am J Surg* 1992; **164**: 337–40.

24 Uden P, Aspelin P, Berglund J *et al.* Preoperative localization in unilateral parathyroid surgery. A cost–benefit study on ultrasound, computed tomography and scintigraphy. *Acta Chir Scand* 1990; **156**: 29–35.

25 Zmora O, Schachter PP, Heymen Z, Shabtay M, Avigad I, Ayalon A. Correct preoperative localization: does it permit a change in operative strategy for primary hyperparathyroidism? *Surgery* 1995; **118**: 932–5.

26 Serpell JW, Campbell PR, Young AE. Preoperative localization of parathyroid tumours does not reduce operative time. *Br J Surg* 1991; **78**: 589–90.

27 Kairaluoma MV, Kellosalo J, Makarainen H, Haukipuro K, Kairaluoma MI. Cost effectiveness of preoperative ultrasound in primary parathyroid surgery. *Ann Chir Gynaecol* 1994; **83**: 279–83.

28 Carlson GL, Farndon JR, Clayton B *et al.* Thallium isotope scintigraphy and ultrasonography: comparative studies of localization techniques in primary hyperparathyroidism. *Br J Surg* 1990; **77**: 327–9.

29 Lloyd MN, Lees WR, Milroy EJ. Pre-operative localisation in primary hyperparathyroidism. *Clin Radiol* 1990; **41**: 239–43.

30 Kairaluoma MV, Makarainen H, Kellosalo J, Haukipuro K, Kairaluoma MI. Results of surgery in primary hyperparathyroidism. *Ann Chir Gynaecol* 1992; **81**: 309–15.

31 Tsukamoto E, Russell CF, Ferguson WR, Laird JD. The role of pre-operative thallium–technetium subtraction scintigraphy in the surgical management of patients with solitary parathyroid adenoma. *Clin Radiol* 1995; **50**: 677–80.

32 Edis AJ, Beahrs OH, van Heerden JA, Akwari OE. 'Conservative' versus 'liberal' approach to parathyroid neck exploration. *Surgery* 1977; **82**: 466–73.

33 Oertli D, Richter M, Kraenzlin M *et al.* Parathyroidectomy in primary hyperparathyroidism: preoperative localization and routine biopsy of unaltered glands are not necessary. *Surgery* 1995; **117**: 392–6.

34 Paloyan E, Lawrence AM, Oslapas R, Shah KH, Ernst K, Hofmann C. Subtotal parathyroidectomy for primary hyperparathyroidism. *Arch Surg* 1983; **118**: 425–31.

35 Molinari AS, Irvin GL 3rd, Desiro GT, Bott L. Incidence of multiglandular disease in primary hyperparathyroidism determined by parathyroid hormone secretion. *Surgery* 1996; **120**: 934–6.

36 Irvin GL, Dembrow VD, Prudhomme DL. Clinical usefulness of an intraoperative 'quick parathyroid hormone' assay. *Surgery* 1993; **114**: 1019–22.

37 Irvin GL, Prudhomme DL, Deriso GT, Sfakianakis G, Chandarlapaty SKC. A new approach to parathyroidectomy. *Ann Surg* 1994; **219**: 574–81.

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